HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B35, 4/21 (19%) recognized this epitope.				
RT (175–183)	Pol	NPDIVIYQY	HIV-1 infection	human (B35)	Sabbaj2002a
	Keywords mother-to-infant transmission. **Donor HLA** A3, A11, B35, B51. • IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope NPDIVIYQY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
RT (175–183)	Pol	HPDIVIYQY	HIV-1 infection, Vaccine	human, macaque (B35)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (175–184)	RT (175–184 LAI)	NPDIVIYQYM	HIV-1 infection	human (B51)	Samri2000
	• This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors. • Patient 246#1 (B51), was found by ELISPOT to recognize the wild type and the mutated peptide after zidovudine treatment. • The resistance mutation M184V gave an increased predicted binding score to B51 (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence and also an increased ELISPOT reactivity.				
RT (175–199)	RT (342–366 LAI)	NPDIVIYQYMDDLYVGSDL-EIGQHR	HIV-1 infection	human (A11)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study.				
RT (179–187)	RT	VIYQYMDDL	Vaccine	human (A*0201)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia • This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.				
RT (179–187)	RT	VIYQYMDDL	HIV-1 infection	human (A*0201)	Tan1999
	• Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts.				

CTL

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable.				
RT (179–187)	Pol (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Sewell1999
	Keywords epitope processing, immunodominance, escape. • Proteasome regulation influences epitope processing and could influence patterns of immunodominance. • The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome. • IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways. • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway. • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Harrer1996a, Menendez-Arias1998
	Keywords review. • The substitution VIYQYVDDL abrogates CTL response and confers drug resistance. • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Frahm2004
	• C. Brander notes this is an A*0201 epitope.				
RT (179–187)	RT (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Brander1998a, Menendez-Arias1998
	Keywords review, escape. • Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape. • Only one subject had CTL against all three epitopes. • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area. • In the review [Menendez-Arias1998] the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) – substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC – substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors.				
RT (179–187)	RT	VIYQYMDDL	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** RT VL9. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, including RT VL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	RT (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Dela Cruz2000

Epitope name VL9.

- Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL.
- These antigens could also be used to stimulate primary responses *in vitro*.

RT (179–187)	Pol (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Sewell2002

Keywords epitope processing, immunodominance.

- Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing.
- ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.

RT (179–187)	Pol	VIYQYMDDL	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002

Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].

RT (179–187)	RT (179–187)	VIYQYMDDL	Vaccine	mouse (A*0201)	Okazaki2003

Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12
Keywords binding affinity, vaccine-induced epitopes.
Assay type cytokine production, Chromium-release assay.
Donor HLA A2.1.

- Alanine substitutions of VIYQYMDDL were tested for importance of each amino acid for HLA-A2.1 binding. Peptide variant (vLyqymddV) showed an 8 fold higher MHC binding affinity than wild type. YLyqymddV had an even higher binding affinity, but the Y at positions one blocked TCR recognition. The higher affinity form of vLyqymddV induced CTL *in vivo* that could protect against a vaccinia virus expressing RT and the wild type epitope.

RT (179–187)	RT	VIYQYMMDL	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a

Keywords inter-clade comparisons.

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A and D consensus sequences are both VIYQYMMDL.

CTL

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	Pol (346–354)	VIYQYMDDL	Vaccine	human (A2)	Woodberry1999

Vaccine *Vector/Type:* DNA prime with vaccinia boost

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-$2D^d$ – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- VIYQYMDDL was recognized by 3 of the HLA-A2 patients.

RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Schmitt2000

Keywords escape, immunotherapy.

- The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL.
- 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL.
- This suggests immunotherapy stimulating anti-VIYQYVDDL responses maybe helpful for reducing lamivudine escape.

RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Haas1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)

RT (179–187)	Pol (339–347 93TH253 subtype CRF01)	VIYQYMDDL	HIV-1 infection	human (A2)	Sriwanthana2001

Keywords HIV exposed persistently seronegative (HEPS).
Epitope name P334-342.

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

RT (179–187)	Pol (339–347 93TH253 subtype CRF01)	VIYQYMDDL	HIV-1 infection	human (A2)	Bond2001

Keywords inter-clade comparisons.

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 2/4 tested FSWs recognized the E clade version of this epitope, which is identical to the previously defined B clade version VIYQYMDDL.
- This epitope was conserved in many subtypes, and exact matches were very uncommon.

RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Day2001

Keywords rate of progression, acute infection.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CTL response to optimally defined CTL epitopes restricted by HLA class 1 A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
RT (179–187)	Pol (346–354 LA1)	VIYQYMDDL	HIV-1 infection	human (A2)	Kelleher2001a
	Keywords HAART, epitope processing. • Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context. • RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome. • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
RT (179–187)	Pol (334–)	VIYQYMDDL	HIV-1 infection	human (A2)	Corbet2003
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol334. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • 1/17 HIV-infected HLA-A2+ people in this study recognized this epitope.				
RT (179–187)	Pol (subtype B)	VIYQYMMDL	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B and D clade viruses.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR26. • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.				

CTL

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
RT (179–187)	RT (346–354 LAI) **Vaccine** *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30 **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR26. • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macrophages in the spleen.	VIYQYMDDL	Vaccine	mouse (A2.1)	Peter2002
RT (180–189)	RT (LAI) • Recognized by CTL from a progressor, spans important RT functional domain. • A previous study determined that this was an epitope recognized by a long-term survivor.	IYQYMDDLYV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, vanderBurg1997
RT (181–189)	RT (181–189 LAI) **Keywords** binding affinity, computational epitope prediction. • This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors. • High levels of recognition by ELISPOT were observed for zidovudine induced mutation YQYVDDLYV and for the wildtype peptide YQYMDDLYV in patient 250#0 (HLA-A*0201), but neither were recognized by patient 201#5 (also HLA-A*0201) • Both the wild-type and the mutated peptide were computer predicted to have a high binding affinity for A2 (http//bimas.dcrt.nih.gov/molbio/hla_bind)	YQYMDDLYV	HIV-1 infection	human (A*0201)	Samri2000
RT (192–201)	RT (192–201) • Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.	DLEIGQHRTK	HIV-1 infection	human (A3)	Haas1998
RT (192–216)	RT (359–383 HXB2) • One of five epitopes defined for RT-specific CTL clones in this study.	DLEIGQHRTKIEELRQHLL-RWGLTT	HIV-1 infection	human (Bw60)	Menendez-Arias1998, Walker1989
RT (192–216)	RT (191–215) **Keywords** HAART, escape. • Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably the escape variant, RT T215Y.	DLEIGQHRTKIEELRQHLL-RWGFTT	HIV-1 infection	human (polyclonal)	Haas1997, Menendez-Arias1998
RT (198–212)	RT (SF2) • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.	HRTKIEELRQHLLRW	HIV-1 infection	human	Altfeld2000b